

**REMARKS**

This is in response to the Office Action mailed November 15, 2006 in the above-identified application. A three-month extension of time for response is requested and the required fee is enclosed.

The present application is directed to glycosylated human interferon alpha isoforms having increased stability in vivo.

Claims 1, 2, and 6-9 are pending and under examination. Claims 3-5 and 10 are withdrawn from consideration.

By this amendment, Claims 1, 2 and 6-9 have been canceled and Claims 11-15 have been added to more particularly define the present invention. Claims 11-15 are supported by the specification, inter alia, at paragraphs 44, 50, 53, 80 and 106-120. Thus, the amendments do not constitute new matter.

The Examiner has objected to Figure 8 as being unclear and providing no useful information. A replacement Figure 8 is enclosed which, applicants submit, should overcome the objection.

Claims 1, 2, 6, 7 and 9 have been rejected. These claims have been canceled and replaced by new Claims 12-15.

Claim 8 has been objected but deemed allowable if rewritten in independent form. Claim 8 has been replaced by new Claim 11 which should be allowable.

Claims 1 and 2 have been rejected under 35 USC §112 ¶1 as lacking enablement for the full scope of the claims. Claims 1 and 2 have been canceled, and replaced by Claims 11-15.

Applicants maintain that new Claims 11-15 are fully enabled by the specification. Claims 11-15 define human interferon alpha isoforms having the amino acid sequence of SEQ ID NO: 1 (admittedly enabled by the Examiner in the Office Action) in which certain defined amino acid substitutions have been made to provide increased in vivo stability. Claim 11 has essentially the same scope as original Claim 8 which the Examiner has deemed allowable.

The modifications in SEQ ID NO: 1 in each of the claims is as follows:

|          |   |
|----------|---|
| Claim 11 | His 34 → Asn; Phe 36 → Ser                                    |
| Claim 12 | His 34 → Asn; Phe 36 → Ser; Leu 26 → Asn                      |
| Claim 13 | His 34 → Asn; Phe 36 → Ser; Lys 134 → Asn                     |
| Claim 14 | His 34 → Asn; Phe 36 → Ser; Leu 26 → Asn and<br>Lys 134 → Asn |

The specification clearly teaches each of these isoforms and their preparation (e.g. paragraphs 106-120) as well as showing they have increased stability (e.g. Figures 8 and 9). In view of the amendments herein, Applicants maintain that the rejection of Claims 1 and 2 as lacking enablement is obviated and that the isoforms defined by Claims 11-15 are clearly enabled and, thus, allowable.

Claims 1 and 2 have been rejected as lacking an adequate written description. The Examiner has alleged that applicants did not have possession of the claimed subject matter at the time of filing.

In view of the amendments to the claims, Applicants maintain that they are clearly in possession of the presently claimed invention. The interferon alpha isoforms of Claims 11-15 are clearly described in the present application in a way showing that the

inventors had possession of the claimed subject matter. Applicants, thereby, request that the lack of adequate written description rejection be withdrawn.

Claims 1 and 2 have been rejected under 35 USC §103(a) as obvious over Nyman et al. in view of U.S. Patent No. 6,309,118 to Margolin et al.

Nyman teaches an interferon alpha isoform (IFN -  $\alpha$  - 14c) that has a glycosylation site at Asn 72. Margolin et al. teach carbohydrate moieties attached to glycoproteins through the hydroxyl side chains of threonine and serine or through the amide nitrogen side chain of asparagine. Margolin et al. also teaches that the addition of such carbohydrate moieties help to increase the stability of the protein.

However, the combination of Nyman and Margolin neither teaches nor suggests the presently claimed interferon alpha isoforms. Indeed, the Examiner indicates that original Claim 8 which corresponds to present Claim 11 is patentable. In view of the amendments to the claims, Applicants maintain that the obviousness rejection of Claims 1 and 2 over Nyman in view of Margolin has been obviated and that Claims 11-15 are allowable.

Claims 6, 7 and 9 have been rejected as obvious over Goeddel et al. (U.S. Pat. No. 6,482,613) in view of Sekellick et al. (U.S. Pat. No. 6,020,465) and Apweiler et al.

Goeddel provides a recombinant human interferon alpha isoform in *E. coli*: (which would not be glycosylated). The glycosylation motif "NXS/T" is not provided. Apweiler provides the glycosylation motif NXS/T (where X is any amino acid except Proline) required for glycosylation of a protein. Sekellick teaches that glycosylated proteins may be recombinantly produced in CHO cells and that N-glycosylation increases stability.

Appln. No. 10/653,350  
Reply to Office Action of November 15, 2006  
Response dated May 15, 2007

Applicants maintain, however, that the combination of these references neither teach nor suggest the presently claimed interferon alpha isoforms (as already acknowledged by the Examiner in indicating that original Claim 8 constituted allowable subject matter). In view of the present amendments, Applicants assert that the obviousness rejection over the combination of Goeddel, Apweiler and Sekellick has been obviated and that Claims 11-15 should be allowed.

Applicants maintain that, in view of the amendments and remarks herein, Claims 11-15 constitute allowable subject matter. A Notice of Allowance is respectfully requested.

This paper is submitted in response to the Office Action dated November 15, 2006.

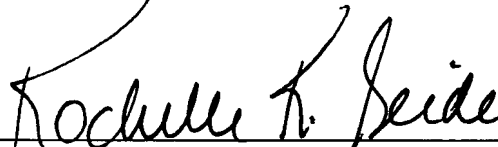
A three-month extension of time for response is respectfully requested. Payment of the extension fee is to be made by Credit Card. Applicants believe that no additional fees are required in connection with this response. However, if additional fees are required, the Commissioner is hereby authorized to charge any additional payment, or credit any overpayment, to Deposit Account No. 01-2300, **referencing Docket Number 027707.00017.**

Appln. No. 10/653,350

Reply to Office Action of November 15, 2006

Response dated May 15, 2007

Respectfully submitted,

A handwritten signature in black ink, reading "Rochelle K. Seide". The signature is written in a cursive style with a large, sweeping initial "R".

Rochelle K. Seide, Ph.D.

Registration No. 32,300

ARENT FOX LLP

1675 Broadway

New York, NY 10019

Tel. No. (212) 484-3945

Fax No. (212) 484-3990

Customer No. 38485

**FEE CALCULATION**

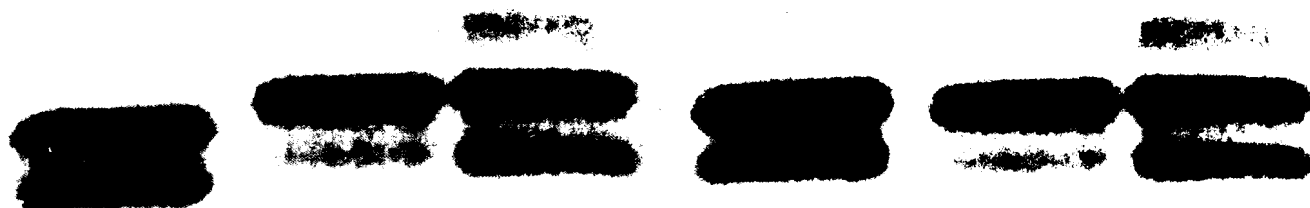
Any additional fee required has been calculated as follows:

\_\_\_ If checked, "Small Entity" status is claimed.

|  | (Column 1)                                | (Column 2)                            | (Column 3)       | SMALL ENTITY |              | OR | LARGE ENTITY |              |
|--|---|---------------------------------------|------------------|--------------|--------------|----|--------------|--------------|
|  | CLAIMS<br>REMAINING<br>AFTER<br>AMENDMENT | HIGHEST NO.<br>PREVIOUSLY<br>PAID FOR | PRESENT<br>EXTRA | RATE         | ADD'L<br>FEE |    | RATE         | ADD'L<br>FEE |
| TOTAL CLAIMS   | 6 MINUS                                   | 20                                    | = 0              | x \$25       | \$           |    | x \$50       | \$0.00       |
| INDEP CLAIMS   | 2 MINUS                                   | 3                                     | = 0              | x \$100      | \$           |    | x \$200      | \$0.00       |
| <input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEP. CLAIM |   |                                       |                  | + \$180      | \$           | OR | + \$360      | \$0.00       |
|  |   |                                       |                  |              | \$           |    |              | \$0.00       |

The U.S. Patent and Trademark Office is hereby authorized to charge and deficiency or credit any overpayment of fees associated with this communication to Deposit Account No. 01-2300 referencing docket number 027707.00017.

1 2 3 4 5 6 7



1. Marker
2. O-Glycosylated IFN-alpha
3. L26N
4. L26N/H34NF36S
5. H34NF36S
6. K134N
7. L26N/K134N